

Amendments to the Claim:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A vaccine composition comprising ~~an isolated protein belonging to the Bcl-2 protein family or an immunogenically active peptide fragment hereof or a nucleic acid encoding said protein or said peptide fragment for use as a medicament,~~ wherein the peptide consists of at the most 15 amino acids and comprises SEQ ID NO:8 or a sequence which differs from SEQ ID NO:8 by one or two amino acid substitutions.

2. (Original) The composition of claim 1, wherein the vaccine composition when administered to a cancer patient, is capable of eliciting an immune response against the cancer disease.

3. (Previously Presented) The composition of claim 1, wherein the vaccine composition, when administered to a cancer patient where a Bcl-2 protein family member is expressed, is capable of eliciting an immune response against the cancer disease.

4-6 (Cancelled).

7. (Currently Amended) The vaccine composition of claim 1, wherein the ~~protein peptide~~ is a fragment of Bcl-2.

8-9 (Cancelled).

10. (Currently Amended) An isolated immunogenically active peptide ~~fragment derived from a protein belonging to the Bcl-2 protein family, and useful as a medicament in the prevention or treatment of a cancer,~~ wherein the peptide consists of at the most 15 amino acids and comprises SEQ ID NO:8 or a homologue thereof differing from SEQ ID NO:8 by one or two amino acid substitutions.

11-12 (Cancelled).

13. (Currently Amended) The peptide ~~fragment~~ according to claim 10 ~~11~~, wherein the peptide is a fragment of protein ~~is Bcl-2~~.

14-15 (Cancelled).

16. (Currently Amended) The peptide ~~fragment~~ according to claim 10 that is capable of eliciting a cellular immune response in a cancer patient.

17. (Currently Amended) The peptide ~~fragment~~ according to claim 10, which is an MHC Class I-restricted peptide having at least one of the following characteristics:

(i) capable of binding to the Class I HLA molecule to which it is restricted at an affinity as measured by the amount of the peptide that is capable of half maximal recovery of the Class I HLA molecule (C_{50} value) which is at the most 50 μ M as determined by the assembly binding assay as described herein,

(ii) capable of eliciting INF- γ -producing cells in a PBL population of a cancer patient at a frequency of at least 1 per 10^4 PBLs as determined by an ELISPOT assay, and/or

(iii) capable of *in situ* detection in a tumor tissue of CTLs that are reactive with the epitope peptide.

18. (Currently Amended) The peptide ~~fragment~~ of claim 17 having a C₅₀ value, which is at the most 30 μ M.

19. (Currently Amended) The peptide ~~fragment~~ of claim 17 having a C₅₀ value, which is at the most 20 μ M.

20. (Currently Amended) The peptide ~~fragment~~ of claim 17, which is restricted by a MHC Class I HLA-A molecule.

21. (Currently Amended) The peptide ~~fragment~~ of claim 20, which is restricted by a MHC Class I HLA species selected from the group consisting of HLA-A1, HLA-A2, HLA-A3, HLA-A11 and HLA-A24.

22. (Currently Amended) The peptide ~~fragment~~ of claim 17, which is restricted by HLA-A2.

23. (Currently Amended) The peptide ~~fragment~~ according to claim 10, which comprises ~~a sequence selected from the group consisting of ALVGACITL (SEQ ID NO:1), ALSPVPPVV (SEQ ID NO:2), SLALVGACI (SEQ ID NO:3), KTLTSLALV (SEQ ID NO:4), LLSLALVGA (SEQ ID NO:5), WLSLKTLLSL (SEQ ID NO:6), AAAGPALSPV (SEQ ID NO:7), PLFDFSWLSL (SEQ ID NO:8), FTARGRFATV (SEQ ID NO:9), YLNRLHLNTWI (SEQ ID NO:10), and NIALWMTEYL (SEQ ID NO:11).~~

24-28 (Cancelled).

29. (Withdrawn-Currently Amended) The peptide ~~fragment~~ of claim 17, which is restricted by a MHC Class I HLA-B molecule.

30. (Withdrawn-Currently Amended) The peptide ~~fragment~~ of claim 29, which is restricted by a MHC Class I HLA-B species selected from the group consisting of HLA-B7, HLA -B35, HLA -B44, HLA-B8, HLA-

USSN - 10/580,016

B15, HLA-B27 and HLA-B51.

31-32 (Cancelled).

33. (Currently Amended) The peptide ~~fragment~~ of claim 10 32, which is a ~~nonapeptide or a decapeptide~~.

34-36 (Cancelled).

37. (Currently Amended) The peptide ~~fragment~~ according to claim 10 comprising, for each specific HLA allele, any of the amino acid residues as indicated in the following table:

HLA allele	Positi on 1	Positi on 2	Positi on 3	Positi on 5	Positi on 6	Positi on 7	C-termin al
HLA-A1		T,S	D,E			L	Y
HLA-A2		L, M			V		L,V
HLA-A3		L,V,M	F,Y				K, Y, F
HLA-A11		V,I,F, Y	M,L,F, Y,I				K, R
HLA-A23		I,Y					W,I
HLA-A24		Y		I,V	F		I,L,F
HLA-A25		M,A,T	I				W
HLA-A26	E,D	V,T,I, L,F			I,L,V		Y,F
HLA-A28	E,D	V,A,L					A,R
HLA-A29		E					Y,L
HLA-A30		Y,L,F, V					Y
HLA-A31			L,M,F, Y				R
HLA-A32		I,L					W

USSN - 10/580,016

HLA-		Y, I, L,				R
A33		V				
HLA-		V, L				R
A34						
HLA-	E, D	T, V				R, K
A66						
HLA-	E, D	T, V				R, K
A68						
HLA-		V, T, A				V, L
A69						
HLA-		T				V, L
A74						
HLA-B5		A, P	F, Y			I, L
HLA-B7	R, A	P				L, F
HLA-B8			K	K, R		L
HLA-		R, K				L, V
B14						
HLA-		Q, L, K,				F, Y, W
B15		P, H, V,				
(B62)		I, M, S,				
		T				
HLA-						L, V
B17						
HLA-		R				Y,
B27						K, F, L
HLA-		P				I, L,
B35						M, Y
HLA-		D, E				I, L, M
B37						
HLA-		H	D, E			F, L
B38						
HLA-		R, H				L, F
B39						
HLA-		E	F, I, V			L, V, A,
B40						W, M, T,
(B60, 6						R
1)						
HLA-		L, P				Y, L
B42						
HLA-		E				F, Y, W
B44						
HLA-		M, I, L,				Y, F

B46 HLA-	V Q, K					L
B48 HLA-	A, P, G					F, Y, I,
B51 HLA-	Q	F, Y				V I, V
B52 HLA-	P					W, F, L
B53 HLA-	P					
B54 HLA-	P					A, V
B55 HLA-	P					A, V
B56 HLA-	A, T, S					F, W, Y
B57 HLA-	A, T, S					F, W, Y
B58 HLA-	P					L
B67 HLA-	R					P
B73 HLA-	A, L					L
Cw1 HLA-	A, L					F, Y
Cw2 HLA-	A, L					L, M
Cw3 HLA-	Y, P, F					L, M, F,
Cw4 HLA-	Y					Y L, Y, F,
Cw6 HLA-	Y					Y L, I,
Cw8 HLA-	A, L					L, V
Cw16						

38. (Currently Amended) The peptide ~~fragment~~ according to claim 10 that is capable of eliciting INF- γ -producing cells in a PBL population of a cancer patient at a frequency of at least 10

USSN - 10/580,016

per 10^4 PBLs.

39. (Currently Amended) The peptide ~~fragment~~ according to claim 10 which is capable of eliciting INF- γ -producing cells in a PBL population of a patient having a cancer disease where a protein belonging to the Bcl-2 protein family is expressed.

40. (Currently Amended) The peptide ~~fragment~~ of claim 39 where the cancer disease is selected from the group consisting of a haematopoietic malignancy, melanoma, breast cancer, cervix cancer, ovary cancer, lung cancer, colon cancer, pancreas cancer and prostate cancer.

41. (Currently Amended) The vaccine composition according to claim 1 comprising a peptide ~~fragment~~ which is an isolated immunogenically active peptide ~~fragment~~ derived from a protein belonging to the Bcl-2 protein family.

42. (Currently Amended) The vaccine composition of claim 41 wherein said peptide ~~fragment~~ has a C_{50} value which is at the most 30 μ M.

43. (Previously Presented) The vaccine composition according to claim 1 where the vaccine elicits the production in a vaccinated patient of effector T-cells having a cytotoxic effect against the cancer cells.

44. (Previously Presented) The vaccine composition according to claim 1 further comprising an immunogenic protein or peptide fragment selected from a protein or peptide fragment not belonging to or derived from the Bcl-2 protein family.

45. (Original) The vaccine composition of claim 44 where the protein or peptide fragment not belonging to or derived from the Bcl-2 protein family is a protein involved in regulation of cell apoptosis or a peptide fragment derived therefrom.

46. (Previously Presented) The vaccine composition of claim 44 where the immunogenic protein or peptide fragment selected from a protein or peptide fragment not belonging to or derived from the Bcl-2 protein family is survivin or a peptide fragment thereof.

47. (Previously Presented) The vaccine composition of claim 44 where the immunogenic protein or peptide fragment selected from a protein or peptide fragment not belonging to or derived from the Bcl-2 protein family is ML-IAP or a peptide fragment thereof.

48. (Previously Presented) The vaccine composition according to claim 1, wherein the composition comprises an adjuvant.

49. (Original) The vaccine composition according to claim 48, wherein the adjuvant is selected from the group consisting of bacterial DNA based adjuvants, oil/surfactant based adjuvants, viral dsRNA based adjuvants and imidazochinilines.

50. (Withdrawn-Currently Amended) The vaccine composition according to claim 1, wherein the vaccine composition comprises antigen presenting cells comprising the ~~protein or peptide fragment~~ or nucleic acid.

51. (Withdrawn) The vaccine composition according to

USSN - 10/580,016

claim 50, wherein the antigen presenting cell is a dendritic cell.

52. (Previously Presented) The vaccine composition according to claim 1, wherein the composition comprises a liposome.

53 (Cancelled).

54. (Withdrawn) The vaccine composition according to claim 1, wherein the nucleic acid is comprised within a vector.

55. (Withdrawn) The vaccine composition according to claim 54, wherein the vector is selected from the group consisting of viral vectors and bacterial vectors.

56. (Withdrawn) The vaccine composition according to claim 54, wherein the vector furthermore comprises nucleic acids encoding a T-cell stimulatory polypeptide.

57. (Withdrawn) The vaccine composition according to claim 56, wherein the T-cell stimulatory polypeptide is selected from the group consisting of B7.1, ICAM-1 and LFA-3.

58. (Previously Presented) A kit-of-parts comprising the vaccine composition according to claim 1, and a further anti-cancer agent.

59. (Previously Presented) The kit-of-parts according to claim 58, wherein the anti-cancer agent is an antibody.

60. (Original) The kit-of-parts according to claim 59, wherein the anti-cancer agent is a cytokine.

61. (Currently Amended) A composition for *ex vivo* or *in situ* diagnosis of the presence in a cancer patient of T cells in PBL or in tumor tissue that are reactive with a Bcl-2 protein family member, the composition comprising a peptide ~~fragment~~ according to claim 10.

62. (Currently Amended) A diagnostic kit for *ex vivo* or *in situ* diagnosis of the presence in a cancer patient of T cells in PBL or in tumor tissue that are reactive with a Bcl-2 protein family member, the kit comprising a peptide ~~fragment~~ according to claim 10.

63. (Currently Amended) A complex of a peptide ~~fragment~~ according to claim 10 and a Class I HLA molecule or a fragment of such molecule.

64. (Original) The complex of claim 63 which is monomeric.

65. (Original) The complex of claim 63 which is multimeric.

66. (Withdrawn) A method of detecting in a cancer patient the presence of a Bcl-2 protein family member reactive T-cells, the method comprising contacting a tumor tissue or a blood sample with a complex of claim 63 and detecting binding of the complex to the tissue or the blood cells.

67-70 (Cancelled).

71. (Withdrawn) A method of treating a cancer disease, the method comprising administering to a patient suffering from the disease an effective amount of the composition according to claim 1.

72. (Withdrawn) The method of claim 71 wherein the disease to be treated is a cancer disease where a Bcl-2 protein family member is expressed.

73. (Withdrawn) The method of claim 71 wherein the cancer disease is selected from the group consisting of a haematopoietic malignancy, melanoma, breast cancer, cervix cancer, ovary cancer, lung cancer, colon cancer, pancreas cancer and prostate cancer.

74. (Withdrawn) The method of to claim 71, which is combined with a further cancer treatment.

75. (Withdrawn) The method of claim 71 wherein the further treatment is selected from the group consisting of chemotherapy, radiotherapy, treatment with immunostimulating substances, gene therapy, treatment with antibodies and treatment using dendritic cells .

76-80. (Cancelled)

81. (Withdrawn-Currently Amended) A method of monitoring immunisation, said method comprising the steps of

- i) providing a blood sample from an individual;
- ii) providing ~~a protein belonging to the Bcl-2 protein family or a peptide fragment~~ according to claim 10; hereof

USSN - 10/580,016

iii) determining whether said blood sample comprises antibodies or T-cells comprising T-cell receptors specifically binding the ~~protein~~ or peptide fragment; and
iv) thereby determining whether an immune response to said ~~protein~~ or peptide fragment has been raised in said individual.

82-83 (Cancelled).

84 (New). The peptide of claim 10 which consists of SEQ ID NO:8.

85 (New). The vaccine composition of claim 1, wherein the peptide is capable of raising a Bcl2-specific T-cell response.

86 (New). The peptide of claim 23 which is a fragment of Bcl-2.

87 (New). The peptide of claim 10 which comprises a sequence which differs from SEQ ID NO:8, if at all, by a single amino acid substitution.

88 (New). The peptide of claim 10, which comprises a sequence which differs from SEQ ID NO:8, if at all, only at residues other than residues 2, 6 and 10 of SEQ ID NO:8.

89 (New). The peptide of claim 10, which comprises a sequence which, if it differs from SEQ ID NO:8, nonetheless is such that the residue corresponding to residue 2 of SEQ ID NO:8

USSN - 10/580,016

is L or M, and the residue corresponding to residue 10 of SEQ ID NO:8 is L or V.

90 (New). The peptide of claim 10, which, if it differs from SEQ ID NO:8, at least one such difference is that the residue corresponding to residue 6 of SEQ ID NO:8 is V.

91 (New). The peptide of claim 87, which comprises a sequence which differs from SEQ ID NO:8, if at all, only at residues other than residues 2, 6 and 10 of SEQ ID NO:8.

92 (New). The peptide of claim 87, which comprises a sequence which, if it differs from SEQ ID NO:8, nonetheless is such that the residue corresponding to residue 2 of SEQ ID NO:8 is L or M, and the residue corresponding to residue 10 of SEQ ID NO:8 is L or V.

93 (New). The peptide of claim 10, which, if it differs from SEQ ID NO:8, said difference is that the residue corresponding to residue 6 of SEQ ID NO:8 is V.